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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/076,937	02/15/2002	Herbert M. Dean	dean0202con	3941

23580 7590 07/18/2007

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EXAMINER	
HUI, SAN MING R	

ART UNIT	PAPER NUMBER
1617	

MAIL DATE	DELIVERY MODE
07/18/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/076,937	DEAN ET AL.	
	Examiner	Art Unit	
	San-ming Hui	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 May 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-18* is/are pending in the application.

4a) Of the above claim(s) *11-16* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-10,17 and 18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's response filed May 14, 2007 have been entered.

No claims are amended.

Claims 1-18 are pending. Claims 11-16 are withdrawn from consideration as they are directed to non-elected invention.

Claims 1-10 and 17-18 are examined to the extent they read on the elected invention.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-10 and 17-18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Pearle (American Heart Journal, 1990 Sep; 120(3):739-742), Carruthers et al. (American Journal of Cardiology, 1993;71:575-581), Abby et al. (Journal of the American Board of Family Practice, 1998; 11(5):391-398), Oakley et al.

(The Journal of Nutrition, 1996;126(3): 751S – 755S), and Behounek et al. (US Patent 5,691,375) in view of Rork et al. (US Patent 5,882,682), references of record.

Pearle teaches that beta-blockers such as timolol, metoprolol, atenolol, and propranolol reducing the overall mortality and the incidence of recurrent myocardial infarction (See the abstract; also page 740, col. 1, second paragraph).

Carruthers et al. teaches atenolol reducing the risk of coronary heart disease (See the abstract).

Abby et al. teaches folic acid and vitamin B_6 are useful in reducing the risk of coronary heart disease such nonfatal myocardial infarction and fatal coronary heart disease (See particularly page 395, Table 2).

Oakley et al. teaches vitamin B_{12} supplement is useful with folic acid administration to avoid the folic acid adverse effect: B_{12} deficiency (See page 3, third and fourth paragraph).

Behounek et al. teaches HMG-CoA reductase inhibitor such as pravastatin is useful in reduce the risk of cardiovascular event (See the abstract).

The references do not expressly the incorporation of beta-blockers such as timolol, metoprolol, atenolol, and propranolol, HMG-CoA reductase inhibitors such as pravastatin, folic acid, vitamin B_6, and vitamin B_{12} into a single once-a-day dosage unit.

Rork et al. teaches a sustained release system that can include beta-bloackers such as timolol, metoprolol, atenolol, and propranolol and statin cholesterol lowering agents such as simvastatin, pravastatin, and lovastatin (See col. 6, line 64-66 and col. 7, line 16).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to incorporate beta-blockers such as timolol, metoprolol, atenolol, and propranolol, HMG-CoA reductase inhibitors such as pravastatin, folic acid, vitamin B_6, and vitamin B_{12} into a single once-a-day dosage unit.

One of ordinary skill in the art would have been motivated to incorporate beta-blockers, such as timolol, metoprolol, atenolol, and propranolol, HMG-CoA reductase inhibitors, such as pravastatin, folic acid, vitamin B_6, and vitamin B_{12} into a single once-a-day dosage unit. All the agents herein: different beta-blockers such as timolol, metoprolol, atenolol, and propranolol, HMG-CoA reductase inhibitors such as pravastatin, folic acid, and vitamin B_6 are all known to reduce risk of cardiovascular diseases. Possessing the teachings of the cited prior art, combining two or more agents which are known to be useful to reduce risk of cardiovascular disease individually into a single sustained release, once-daily composition useful for the very same purpose is prima facie obvious (See *In re Kerkhoven* 205 USPQ 1069), absent evidence to the contrary. Furthermore, possessing the teaching of Oakley et al., one of ordinary skill in the art would incorporate vitamin B_{12} into any folic acid containing composition including the instant composition since vitamin B_{12} administration would prevent folic acid adverse effect such as vitamin B_{12} deficiency.

Response to Arguments

Applicant's arguments filed May 14, 2007 averring the cited prior art's failure to provide motivation or suggestion to accomplish the herein recited use, i.e., compliance

composition, have been fully considered but they are not persuasive. The examiner notes that such arguments are directed to the intended properties of the herein recited composition. The intended benefit is either directed to the intended use. Such limitation does not materially change the makeup of the herein claimed composition. Therefore, the claims are still considered properly rejected by the cited prior art under 35 USC 103(a).

Applicant's arguments filed May 14, 2007 averring the presence of the unexpected benefit have been considered, but are not found persuasive. As discussed in the previous office action mailed November 16, 2006, Examiner notes that the evidences cited by the applicant are published after the effective filing date of the instant application. Such references cannot be probative evidence for establishing non-obviousness. Moreover, and more importantly, when using a single dose combination product, the patient compliance to the dosing regimen is reasonably expected to improve. There are lots of clinical studies investigating and comparing once daily dosing versus multiple daily dosing. These clinical studies are directed to the treatment of various disorders ranging from HIV (cocktail multiple-drug therapy), asthma, depression (a lots of time multiple drugs therapy), hypertension (such as the instant case), and diabetes. Examiner provides two clinical studies that are related to cardiovascular diseases (See Waeber et al., and Mounier-Vehier et al.). In these two studies, it is clear that once daily dosing can improve the patient compliance significantly in 30% of patients, for example. In view of the cited prior arts, one of ordinary skill in the art would therefore reasonably expect the combination product improve the patient compliance.

Accordingly, improvement of patient compliance seen in the instant case is not unexpected. Therefore, the claims are still considered properly rejected by the cited prior art under 35 USC 103(a).

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to San-ming Hui whose telephone number is (571) 272-0626. The examiner can normally be reached on Mon 9:00 to 1:00, Tu - Fri from 9:00 to 6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan, PhD., can be reached on (571) 272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

San-ming Hui
Primary Examiner
Art Unit 1617